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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,026	01/18/2002	Tadashi Mukai	06854.0011	8884

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EXAMINER	
KRASS, FREDERICK F	

ART UNIT	PAPER NUMBER
1614	

DATE MAILED: 02/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,026	MUKAI ET AL.	
	Examiner	Art Unit	
	Frederick F. Krass	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *RCE Request with Arguments (2/2/04)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-10,12-14,20,21,23-26 and 29-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7-10,12-14,20, 21, 23-26 and 29-31* is/are rejected.

7)☒ Claim(s) ____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Previous Rejections

All previous rejections are withdrawn.

The arguments presented by Applicant with the RCE Request are agreed with substantially as written.

Claim Informalities

Claim 1 is poorly constructed, probably because of a literal translation. While not indefinite *per se*, it could certainly stand some revision to place it in better form. The examiner recommends the following:

1. A cilostazol preparation which is capable of dissolving at the lower portion of a human digestive tract, comprising a fine powder of cilostazol having an average particle diameter of 10um or less as an active ingredient, wherein said fine powder has been incorporated into a surfactant as a dispersing and/or solubilizing agent.

Claim Objection, Failure to Further Limit

Claim 21 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 1 (the sole independent claim) already recites the limitation in claim 21 that the preparation "has a capability of dissolving cilostazol even at the lower portion of the digestive tract."

Indefiniteness Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7-10, 12-14, 20, 21, 23-26 and 29-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

i) Claims 29, 30 and 31 are indefinite insofar as they use improper Markush group terminology. Specifically, the partially open term "essentially consisting of" at the second line of each claim is improper; Markush members must be selected from a closed group. This can be readily corrected by deleting the term "essentially" at each occurrence.

ii) Claim 25, the phrase "contain a cilostazol preparation and rapid release powders or tablets containing cilostazol" is confusing. First, "contain a cilostazol preparation" is redundant, since a cilostazol preparation is already claimed; second "and rapid release powders or tablets" is inconsistent with the earlier recitation of a sustained, not rapid, release composition. Clarification and/or correction is required.

iii) Claim 26, the modifying term "type" is indefinite insofar as it is appended to an already definite term, such that its modifying effect is unclear. Since the term is not necessary to an understanding of the claimed subject matter, the examiner recommends deleting it, reciting simply "multiple-unit" preparation" instead.

iv) The term "small" in claim 26 is a relative term which renders the claim indefinite. The term "small" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. The specification provides neither a specific definition of the term "small", nor representative examples of values which would be "small". Since the term is

not necessary to an understanding of the claimed subject matter, the examiner recommends deleting it.

Obviousness Rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 4, 7-10, 12-14 and 29-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Fujimura et al ("Bronchoprotective Effect of an Intrabronchial Administration of Cilostazol Powder and a Nebulized PDE1 and PDE4 Inhibitor KF19514 in Guinea Pigs", *Int. Arch. Allergy Immunol.* vol.116, pp. 220-227 (1998)) in view of Wood et al (USP 6,264,922).

The primary reference discloses the use of cilostazol in aerosolized dry powder form for inhalation therapy. The powder is sized for intrabronchial administration, i.e. has an extremely small particle size on the order of about 3-4 microns. See the passage spanning the bottom righthand side of page 221 to the lefthand top side of page 222. The reference differs from the instant claims insofar as it does not disclose incorporating the powder into a surfactant as a dispersing and/or solubilizing agent.

The secondary reference teaches that the bioavailability of an aerosolized pharmaceutical can be increased by treating the fine particles of active agent with 0.1-90 percent by weight of a surfactant, e.g. sodium lauryl sulfate. See the first paragraph of col. 5 (line 8 in particular); see also the passage spanning the bottom of col. 11 to the top of col. 12 (which teaches that the relative proportions of surfactant and active agent can be optimized depending on the particular agent and application). The reference is particularly concerned with powders sized for intrabronchial administration, i.e. having particle sizes of 10um or less. See col. 1, lines 33-42; see also claim 1. The prior art differs from the instant claims insofar as, although it contemplates a wide variety of active agents (see col. 3, lines 45 et seq.), it does not specifically disclose cilostazol.

It would have been obvious to have treated the cilostazol powder of the primary reference with a surfactant such as lauryl sulfate, motivated by the desire to improve bioavailability as taught by the secondary reference.

The instant limitation "having a capability of dissolving cilostazol even at the lower portion of the digestive tract" is merely a functional characterization of future use which carries no weight in determining patentability. The modified aerosols suggested by the prior art would clearly have that ability were they to be formulated into the proper enteric forms. (This is especially so given that the prior art suggests that surfactant treatment increases solubility: see col. 3, lines 30-44, for example).

Technological Background Material

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

USP 6,825,214 demonstrates the state of the art. The reference discloses finely divided cilastozol powders having a particle size of a low as "less than about 15 microns". See claim 5. Particle sizes lower than 10um are not specified. The reference is also silent regarding surfactants. (USP 6,825,214 does in fact actually teach away from the instant claims, since it requires "substantially pure" cilastozol powder. It is also not available as "prior art" insofar as its effective filing date (8/14/2000) is later than the 371 date of the instant application (3/21/2000)).

Allowable Subject Matter

Claims 20, 21 and 23-26 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

The prior art does not fairly suggest, teach or disclose a cilastozol preparation having a particle size of 10um or less, which has been incorporated into a surfactant as a dispersing and/or solubilizing agent, and coated with a sustained release coating material. The prior art of record in fact teaches away from this concept; the purpose of treating fine powders with surfactants by USP 6,264,922 is to promote immediate, not sustained, release. Conversely, one would not be motivated to use cilastozol having a particle size of 10um or less except when administering the composition in aerosolized form for inhalation. See col. 2, lines 5-15 of the patent. Accordingly, one would not be motivated to use such fine particle size for enteric applications (where sustained release is required), and the prior art would not recognize the unexpected advantages of increased absorption rate in the lower intestine demonstrated by Applicant in the instant working examples.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frederick F. Krass whose telephone number is 571-272-0580. The examiner's schedule is as follows:

Monday: 10:30AM- 7PM;
Tuesday: 10:30AM - 7PM;
Wednesday: off;
Thursday: 10:30AM- 7PM; and
Friday: 10:30AM-7PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frederick Krass
Primary Examiner
Art Unit 1614